IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re the Application of:		)	
	C. Richter King, et al.	)	Group Art Unit: 1643
U.S. Patent No.:	7,838,216	)	Examiner: Rawlings, Stephen L.
Issued:	November 23, 2010	)	Confirmation No.: 7373
Serial No.:	07/110,791	)	REQUEST FOR CERTIFICATE OF CORRECTION
Filed:	October 21, 1987	)	*(filed electronically)*
Atty. File No.:	6137NCI-24	)	
For:	"HUMAN GENE RELATED TO BUT DISTINCT FROM EGF RECEPTOR GENE"	)	

ATTN: Certificate of Corrections Branch
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

This is a request for a Certificate of Correction for PTO mistakes under 37 CFR 1.322(a). Attached is Form PTO SB/44. The errors in the patent are typographical errors or omissions and the correct wording can be found in the supporting documents attached.

1. Column 6, line 32, please replace "CGCTTTTGTTCTGCAAAAACGTATCTCCTAAT" with --CGCTTTTGTTCT**C**GCAAAAACGTATCTCCTAAT--.

Support for correction of this error (insertion of the bolded "C" above) can be found in the Amendment filed on April 4, 1995 (page 9), and attached copy of nucleotide from GenBank X00588.1.

2. Column 7, line 49, please replace "cellulose" with --cellular--.

Support for correction of this error can be found in the Specification as filed on October 21, 1997, page -9a-, line 23 (copy attached as downloaded from PAIR).

3. Column 9, line 55, please replace the line, "for FIG. 2A and 20 min for FIG. 2, 40 min for EGF receptor" with -- for FIG. 2A and 20 min for FIG. 2B, 40 min for EGF receptor --.

Support for correction of this error can be found in the Amendment filed on April 4, 1995 (see page 12).

4. Column 10, line 39, please replace the word "with" with --in--.

Support for correction of this error can be found in the Amendment and Response filed on May 6, 2009 (see page two).

5. Column 11, line 64, please replace the word "in" with --a--.

Support for correction of this error can be found in the Specification as filed, page 19 (copy attached as downloaded from PAIR).

6. Column 12, line 47, please replace the words "whereint he" with --wherein the--.

Support for correction of this error can be found in the Amendment filed May 6, 2009 (see page 4).

7. Column 15, line 63, please replace the words "probe B c in FIG." with --probe c in FIG.--.

Support for correction of this error can be found in the Amendment, filed April 4, 1995 (page 14).

8. Column 16, line 64, please replace the word "increase" with --increased--.

Support for correction of this error can be found in the Amendment, filed April 4, 1995 (page 15).

Respectfully submitted.

SHERIDAN ROSS P.C.

Date: March 11, 2011

By: /Gary J. Connell/

Gary J. Connell
Registration No. 32,020
1560 Broadway, Suite 1200
Denver, Colorado 80202-5141
(303) 863-9700

PTO/SB/44 (09-07)
Approved for use through 08/31/2013. OMB 0651-0033
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.
(Also Form PTO-1050)

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 7,838,216

APPLICATION NO.: 07/110,791

ISSUE DATE : Nov. 23, 2010

INVENTOR(S) : C. Richter King, Matthias H. Kraus and Stuart A. Aaronson

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 6, line 32, replace "CGCTTTTGTTCTGCAAAAACGTATCTCCTAAT" with --CGCTTTTGTTCTCGCAAAAACGTATCTCCTAAT--.

Column 7, line 49, replace "cellulose" with --cellular--.

Column 9, line 55, replace the line, "for FIG. 2A and 20 min for FIG. 2, 40 min for EGF receptor" with --for FIG. 2A and 20 min for FIG. 2B, 40 min for EGF receptor--.

Column 10, line 39, replace the word "with" with --in--.

Column 11, line 64, replace the word "in" with --a--.

Column 12, line 47, replace the words "whereint he" with --wherein the--.

Column 15, line 63, replace the words "probe B c in FIG." with --probe c in FIG.--.

Column 16, line 64, replace the word "increase" with --increased--.

MAILING ADDRESS OF SENDER (Please do not use customer number below):

Sheridan Ross P.C.
1560 Broadway, Suite 1200
Denver, CO 80202-5141

Privacy Act Statement

The **Privacy Act of 1974 (P.L. 93-579)** requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Nucleotide
Alphabet of Life

Display Settings: FASTA

Human mRNA for precursor of epidermal growth factor receptor

GenBank X00588.1

```
>gi|31113|emb|X00588.1| Human mRNA for precursor of epidermal growth factor
receptor
GCCGCGCTGCGCCGGAGTCCCGAGCTAGCCCCGGCGCCGCCGCCGCCCAGACCGGACGACAGGCCACCTC
GTCGGCGTCCGCCCGAGTCCCCGCCTCGCCGCCAACGCCACAACCACCGCGCACGGCCCCCTGACTCCGT
CCAGTATTGATCGGGAGAGCCGGAGCGAGCTCTTCGGGGAGCAGCGATGCGACCCTCCGGGACGGCCGGG
GCAGCGCTCCTGGCGCTGCTGGCTGCGCTCTGCCCGGCGAGTCGGGCTCTGGAGGAAAAGAAAGTTTGCC
AAGGCACGAGTAACAAGCTCACGCAGTTGGGCACTTTTGAAGATCATTTTCTCAGCCTCCAGAGGATGTT
CAATAACTGTGAGGTGGTCCTTGGGAATTTGGAAATTACCTATGTGCAGAGGAATTATGATCTTTCCTTC
TTAAAGACCATCCAGGAGGTGGCTGGTTATGTCCTCATTGCCCTCAACACAGTGGAGCGAATTCCTTTGG
AAAACCTGCAGATCATCAGAGGAAATATGTACTACGAAAATTCCTATGCCTTAGCAGTCTTATCTAACTA
TGATGCAAATAAAACCGGACTGAAGGAGCTGCCCATGAGAAATTTACAGGAAATCCTGCATGGCGCCGTG
CGGTTCAGCAACAACCCTGCCCTGTGCAACGTGGAGAGCATCCAGTGGCGGGACATAGTCAGCAGTGACT
TTCTCAGCAACATGTCGATGGACTTCCAGAACCACCTGGGCAGCTGCCAAAAGTGTGATCCAAGCTGTCC
CAATGGGAGCTGCTGGGGTGCAGGAGAGGAGAACTGCCAGAAACTGACCAAAATCATCTGTGCCCAGCAG
TGCTCCGGGCGCTGCCGTGGCAAGTCCCCCAGTGACTGCTGCCACAACCAGTGTGCTGCAGGCTGCACAG
GCCCCCGGGAGAGCGACTGCCTGGTCTGCCGCAAATTCCGAGACGAAGCCACGTGCAAGGACACCTGCCC
CCCACTCATGCTCTACAACCCCACCACGTACCAGATGGATGTGAACCCCGAGGGCAAATACAGCTTTGGT
GCCACCTGCGTGAAGAAGTGTCCCCGTAATTATGTGGTGACAGATCACGGCTCGTGCGTCCGAGCCTGTG
GGGCCGACAGCTATGAGATGGAGGAAGACGGCGTCCGCAAGTGTAAGAAGTGCGAAGGGCCTTGCCGCAA
AGTGTGTAACGGAATAGGTATTGGTGAATTTAAAGACTCACTCTCCATAAATGCTACGAATATTAAACAC
TTCAAAAACTGCACCTCCATCAGTGGCGATCTCCACATCCTGCCGGTGGCATTTAGGGGTGACTCCTTCA
CACATACTCCTCCTCTGGATCCACAGGAACTGGATATTCTGAAAACCGTAAAGGAAATCACAGGGTTTTT
GCTGATTCAGGCTTGGCCTGAAAACAGGACGGACCTCCATGCCTTTGAGAACCTAGAAATCATACGCGGC
AGGACCAAGCAACATGGTCAGTTTTCTCTTGCAGTCGTCAGCCTGAACATAACATCCTTGGGATTACGCT
CCCTCAAGGAGATAAGTGATGGAGATGTGATAATTTCAGGAAACAAAAATTTGTGCTATGCAAATACAAT
AAACTGGAAAAAACTGTTTGGGACCTCCGGTCAGAAAACCAAAATTATAAGCAACAGAGGTGAAAACAGC
TGCAAGGCCACAGGCCAGGTCTGCCATGCCTTGTGCTCCCCCGAGGGCTGCTGGGGCCCGGAGCCCAGGG
ACTGCGTCTCTTGCCGGAATGTCAGCCGAGGCAGGGAATGCGTGGACAAGTGCAAGCTTCTGGAGGGTGA
GCCAAGGGAGTTTGTGGAGAACTCTGAGTGCATACAGTGCCACCCAGAGTGCCTGCCTCAGGCCATGAAC
ATCACCTGCACAGGACGGGGACCAGACAACTGTATCCAGTGTGCCCACTACATTGACGGCCCCCACTGCG
TCAAGACCTGCCCGGCAGGAGTCATGGGAGAAAACAACACCCTGGTCTGGAAGTACGCAGACGCCGGCCA
TGTGTGCCACCTGTGCCATCCAAACTGCACCTACGGATGCACTGGGCCAGGTCTTGAAGGCTGTCCAACG
AATGGGCCTAAGATCCCGTCCATCGCCACTGGGATGGTGGGGGCCCTCCTCTTGCTGCTGGTGGTGGCCC
TGGGGATCGGCCTCTTCATGCGAAGGCGCCACATCGTTCGGAAGCGCACGCTGCGGAGGCTGCTGCAGGA
GAGGGAGCTTGTGGAGCCTCTTACACCCAGTGGAGAAGCTCCCAACCAAGCTCTCTTGAGGATCTTGAAG
GAAACTGAATTCAAAAAGATCAAAGTGCTGGGCTCCGGTGCGTTCGGCACGGTGTATAAGGGACTCTGGA
TCCCAGAAGGTGAGAAAGTTAAAATTCCCGTCGCTATCAAGGAATTAAGAGAAGCAACATCTCCGAAAGC
CAACAAGGAAATCCTCGATGAAGCCTACGTGATGGCCAGCGTGGACAACCCCCACGTGTGCCGCCTGCTG
GGCATCTGCCTCACCTCCACCGTGCAACTCATCACGCAGCTCATGCCCTTCGGCTGCCTCCTGGACTATG
TCCGGGAACACAAAGACAATATTGGCTCCCAGTACCTGCTCAACTGGTGTGTGCAGATCGCAAAGGGCAT
GAACTACTTGGAGGACCGTCGCTTGGTGCACCGCGACCTGGCAGCCAGGAACGTACTGGTGAAAACACCG
CAGCATGTCAAGATCACAGATTTTGGGCTGGCCAAACTGCTGGGTGCGGAAGAGAAAGAATACCATGCAG
AAGGAGGCAAAGTGCCTATCAAGTGGATGGCATTGGAATCAATTTTACACAGAATCTATACCCACCAGAG
TGATGTCTGGAGCTACGGGGTGACCGTTTGGGAGTTGATGACCTTTGGATCCAAGCCATATGACGGAATC
CCTGCCAGCGAGATCTCCTCCATCCTGGAGAAAGGAGAACGCCTCCCTCAGCCACCCATATGTACCATCG
ATGTCTACATGATCATGGTCAAGTGCTGGATGATAGACGCAGATAGTCGCCCAAAGTTCCGTGAGTTGAT
CATCGAATTCTCCAAAATGGCCCGAGACCCCCAGCGCTACCTTGTCATTCAGGGGGATGAAAGAATGCAT
TTGCCAAGTCCTACAGACTCCAACTTCTACCGTGCCCTGATGGATGAAGAAGACATGGACGACGTGGTGG
ATGCCGACGAGTACCTCATCCCACAGCAGGGCTTCTTCAGCAGCCCCTCCACGTCACGGACTCCCCTCCT
GAGCTCTCTGAGTGCAACCAGCAACAATTCCACCGTGGCTTGCATTGATAGAAATGGGCTGCAAAGCTGT
CCCATCAAGGAAGACAGCTTCTTGCAGCGATACAGCTCAGACCCCACAGGCGCCTTGACTGAGGACAGCA
TAGACGACACCTTCCTCCCAGTGCCTGAATACATAAACCAGTCCGTTCCCAAAAGGCCCGCTGGCTCTGT
GCAGAATCCTGTCTATCACAATCAGCCTCTGAACCCCGCGCCCAGCAGAGACCCACACTACCAGGACCCC
CACAGCACTGCAGTGGGCAACCCCGAGTATCTCAACACTGTCCAGCCCACCTGTGTCAACAGCACATTCG
ACAGCCCTGCCCACTGGGCCCAGAAAGGCAGCCACCAAATTAGCCTGGACAACCCTGACTACCAGCAGGA
CTTCTTTCCCAAGGAAGCCAAGCCAAATGGCATCTTTAAGGGCTCCACAGCTGAAAATGCAGAATACCTA
AGGGTCGCGCCACAAAGCAGTGAATTTATTGGAGCATGACCACGGAGGATAGTATGAGCCCTAAAAATCC
AGACTCTTTCGATACCCAGGACCAAGCCACAGCAGGTCCTCCATCCCAACAGCCATGCCCGCATTAGCTC
TTAGACCCACAGACTGGTTTTGCAACGTTTACACCGACTAGCCAGGAAGTACTTCCACCTCGGGCACATT
TTGGGAAGTTGCATTCCTTTGTCTTCAAACTGTGAAGCATTTACAGAAACGCATCCAGCAAGAATATTGT
CCCTTTGAGCAGAAATTTATCTTTCAAAGAGGTATATTTGAAAAAAAAAAAAAAAAGTATATGTGAGGATT
TTTATTGATTGGGGATCTTGGAGTTTTTCATTGTCGCTATTGATTTTTACTTCAATGGGCTCTTCCAACA
AGGAAGAAGCTTGCTGGTAGCACTTGCTACCCTGAGTTCATCCAGGCCCAACTGTGAGCAAGGAGCACAA
GCCACAAGTCTTCCAGAGGATGCTTGATTCCAGTGGTTCTGCTTCAAGGCTTCCACTGCAAAACACTAAA
GATCCAAGAAGGCCTTCATGGCCCCAGCAGGCCGGATCGGTACTGTATCAAGTCATGGCAGGTACAGTAG
GATAAGCCACTCTGTCCCTTCCTGGGCAAAGAAGAAACGGAGGGGATGAATTCTTCCTTAGACTTACTTT
TGTAAAAATGTCCCCACGGTACTTACTCCCCACTGATGGACCAGTGGTTTCCAGTCATGAGCGTTAGACT
GACTTGTTTGTCTTCCATTCCATTGTTTTGAAACTCAGTATGCCGCCCCTGTCTTGCTGTCATGAAATCA
GCAAGAGAGGATGACACATCAAATAATAACTCGGATTCCAGCCCACATTGGATTCATCAGCATTTGGACC
AATAGCCCACAGCTGAGAATGTGGAATACCTAAGGATAACACCGCTTTTGTTCTCGCAAAAACGTATCTC
```
← correct
```
CTAATTTGAGGCTCAGATGAAATGCATCAGGTCCTTTGGGGCATAGATCAGAAGACTACAAAAATGAAGC
TGCTCTGAAATCTCCTTTAGCCATCACCCCAACCCCCCAAAATTAGTTTGTGTTACTTATGGAAGATAGT
TTTCTCCTTTTACTTCACTTCAAAAGCTTTTTACTCAAAGAGTATATGTTCCCTCCAGGTCAGCTGCCCC
CAAACCCCCTCCTTACGCTTTGTCACACAAAAAGTGTCTCTGCCTTGAGTCATCTATTCAAGCACTTACA
GCTCTGGCCACAACAGGGCATTTTACAGGTGCGAATGACAGTAGCATTATGAGTAGTGTGAATTCAGGTA
GTAAATATGAAACTAGGGTTTGAAATTGATAATGCTTTCACAACATTTGCAGATGTTTTAGAAGGAAAAA
AGTTCCTTCCTAAAATAATTTCTCTACAATTGGAAGATTGGAAGATTCAGCTAGTTAGGAGCCCATTTTT
TCCTAATCTGTGTGTGCCCTGTAACCTGACTGGTTAACAGCAGTCCTTTGTAAACAGTGTTTTAAACTCT
CCTAGTCAATATCCACCCCATCCAATTTATCAAGGAAGAAATGGTTCAGAAAATATTTTCAGCCTACAGT
TATGTTCAGTCACACACACATACAAAATGTTCCTTTTGCTTTTAAAGTAATTTTTGACTCCCAGATCAGT
CAGAGCCCCTACAGCATTGTTAAGAAAGTATTTGATTTTTGTCTCAATGAAAATAAAACTATATTCATTT
```

from orig spec. as filed

Fig. 5A shows the restriction map of complementary DNA of MAC117 encompassing the entire coding region of the gene. Clone pMAC137 was isolated from an oligo dT primed normal human fibroblast cDNA library (Okyama et al., Mol. Cell. Biol. 3, 280, 1983) using a 0.8-kbp Acc I fragment from the 3' terminus of pMAC117 as probe. Clones λMAC30, λMAC10', and λMAC14-1 were subsequently isolated from a randomly primed MCF-7 cDNA library (Walter et al., Proc. Natl. Acad. Sci. USA, 82, 7889, 1985) using cDNA fragments as probes. Restriction sites: B - Bam HI, BII - Bst EII, E - Eco RI, N - NCO I, P - Pst I, Sm - Sma I, Sp - Sph I, and St - Stu I.

Fig. 6 shows the overexpression of MAC117 in RNA in human mammary tumor cell lines. (A) Northern blot analysis. Total cellular RNA (10 μg) of mammary tumor cell lines, normal fibroblasts M413 and HBL100 was hybridized with a cDNA probe derived from the 5' end of the coding region (Fig. 5B, probe a). M413 and HBL100 cells contain specific mRNA detectable after longer autoradiographic exposures. Similar results were obtained when probe b or c (Fig. 5B) was employed for hybridization. (B) Quantitation of mRNA levels. Serial 2-fold dilutions of total RNA were applied to nitrocellulose. Replicate filters were hybridized with either a cDNA probe (Fig. 5B, probe b) or human β-actin which served as control for RNA amounts present on the nitrocelluiose filter. Relative amounts detected with each probe are indicated in comparison to the hybridization signals observed in normal human fibroblast M413.

Fig. 7 shows the 185-kDal protein specific for MAC117 and its overexpression in human mammary tumor cell lines. 40 μg total cellular protein was separated by electrophoresis and transferred to nitrocellulose filters. The protein was detected with an antipeptide antibody coupled to ^{125}I protein A. The

col. 7 line 49

from orig spec as filed

A deposit of pMAC117 cloned in E. coli has been made at the American Type Culture Collection (ATCC), Bethesda, Md. under accession number 53408. Upon issuance of a patent, the culture will continue to be maintained for at least 30 years and made available to the public without restriction subject, of course, to the provisions of the law in this respect.

As shown in Fig. 2A, DNA prepared from tissue of a human mammary carcinoma, MAC117, showed a pattern of hybridization that differed both from that observed with DNA of normal human placenta and from that observed with the A431 squamous-cell carcinoma line, which contains amplified epidermal growth factor (EGF) receptor genes. In A431 DNA, four Eco RI fragments were detected that had increased signal intensities compared to those of corresponding fragments in placenta DNA (Fig. 2A). In contrast, MAC117 DNA contained a single 6-kilobase pair (kbp) fragment, which appeared to be amplified compared to corresponding fragments observed in both A431 and placenta DNA's (Fig. 2A). These findings indicate that the MAC117 tumor contained an amplified DNA sequence related to, but distinct from, the cellular erbB proto-oncogene.

col. 11 line 64

DOCKET NUMBER 1414.025
PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	)	
	)	
KING et al.	)	
	)	Group Art Unit: 1807
Serial No. 07/110,791	)	
	)	Examiner: Marschel, A
Filed: October 21, 1987	)	
	)	
For: HUMAN GENE RELATED TO BUT DISTINCT FROM EGF RECEPTOR GENE	)	

AMENDMENT

Honorable Commissioner of
Patents and Trademarks

Washington, D.C. 20231

NEEDLE & ROSENBERG, P.C.
Suite 1200
The Candler Building
127 Peachtree Street, N.E.
Atlanta, Georgia 30303-1811

April 4, 1995

Sir:

This is responsive to the October 4, 1994 Office Action. A three month Request for Extension of Time is filed herewith. Please amend the above-identified application as follows:

IN THE SPECIFICATION

Please amend the specification as follows:

GGCCTTCATGGCCCCAGCAGGCCGGATCGGTACTGTATCAAGTCATGGCAGGTACAG

TAGGATAAGCCACTCTGTCCCTTCCTGGGCAAAGAAGAAACGGAGGGGATGAATTCT

TCCTTAGACTTACTTTTGTAAAAATGTCCCCACGGT

ACTTACTCCCCACTGATGGACCAGTGGTTTCCAGTCATGAGCGTTAGACTGACTTGTT

TGTCTTCCATTCCATTGTTTTGAAACTCAGTATGCCGCCCCTGTCTTGCTGTCATGAA

ATCAGCAAGAGAGGATGACACATCAAATAATAAC

TCGGATTCCAGCCCACATTGGATTCATCAGCATTTGGACCAATAGCCCACAGCTGAG

AATGTGGAATACCTAAGGATAACACCGCTTTTGTTCTCGCAAAAACGTATCTCCTAAT

TTGAGGCTCAGATGAAATGCATCAGGTCCTTTGGG

COL. 6
LN. 35

GCATAGATCAGAAGACTACAAAAATGAAGCTGCTCTGAAATCTCCTTTAGCCATCAC

CCCAACCCCCCAAAATTAGTTTGTGTTACTTATGGAAGATAGTTTTCTCCTTTTACTTC

ACTTCAAAAGCTTTTTACTCAAAGAGTATATGTT

CCCTCCAGGTCAGCTGCCCCCAAACCCCCTCCTTACGCTTTGTCACACAAAAAGTGTC

TCTGCCTTGAGTCATCTATTCAAGCACTTACAGCTCTGGCCACAACAGGGCATTTTAC

AGGTGCGAATGACAGTAGCATTATGAGTAGTGTG

On page 13, line 14, please delete "1A" and substitute therefor --2A--.

On page 13, line 15, please delete "1AB" and substitute therefor --2B--.

Col. 9
Ln. 55

On page 14, line 2, please delete "Hi" and substitute therefor --HI--.

On page 15, line 16, please delete "(Fig. 2)" and substitute therefor --(Fig. 1)--.

On page 15, line 20, please delete "αP^{12}dXTP" and substitute therefor --α^{32}PdXTP--.

On page 17, line 1, please insert --λ-- before "MAC117".

On page 17, line 11, please delete "dithiothretol" and substitute therefor --dithiothreitol--.

On page 17, line 20, please delete "plaques" and substitute therefor --plates--.

On page 18, line 6, please delete "1" and substitute therefor --2--.

On page 18, line 7, please delete "Fig. 1" and substitute therefor --Fig. 2--.

On page 21, line 16, after "probe" and before "detected", please insert the following: --, consisting of the Bgl I to Bam HI restriction fragment of pMAC117,--.

On page 22a, line 2 and lines 19-20, after "Kraus et al.," and before "1987", please insert the following: --*EMBO Journal* **6**:605-610,--.

On page 22a, line 4, after "from" and before "a", please insert the following: --the 3' terminus of--.

On page 22c, line 6, please delete "(Fig. 5)" and substitute therefor --(Figs. 5A,B)--.

On page 22c, line 9 and page 22d, line 16, after "DiFiore et al.," and before "1987", please insert the following: --*Science* **237**:178-182,--.

On page 22c, lines 22 and 26 and on page 22d, lines 8 and 12, please delete "Table I" and substitute therefor --Table 1--.

On page 24, line 2, please delete "Figures 1" and substitute therefor --Figures 2--.

On page 24, line 28, please delete "C" and substitute therefor --c--.

COL.15
LN. 63

On page 26, line 16, please delete "sequence of claim 4" and substitute therefor --sequence:

GlyMetSerTyrLeuGluAspValArgLeuValHisArgAspLeuAlaAlaARgAsnValLeuValLysSerProAsn HisValLysIleThrAspPheGlyLeuAlaArgLeuLeuAspIleAspGluThrGluTyrHisAlaAspGlyGlyLysVal ProIleLysTrpMetAlaLeuGluSerIleLeuArgArgArgPheThrHisGlnSerAspValTrpSerTyrGly--.

On page 26, lines 17-18, please delete "nove. v-erbB-related gene in" and substitute therefor --novel v-erbB-related gene is--.

On page 27, line 2, please delete "Figures 1" and substitute therefor --Figures 2--.

On page 27, line 5, please delete "5A" and substitute therefor --5B--.

On page 27, line 12, after "amplification" and before "of", please insert the following: --or increased expression--.

COL. 16
LN. 64

On page 27, line 17, after "gene" and before "are", please insert the following: --or its mRNA transcript--.

On page 27, line 19, please delete "Figure 1" and substitute therefor --Figure 2--.

On page 28, line 6, please delete "form" and substitute therefor --from--.

directly contact the undersigned if such contact may enhance the efficient prosecution of this application to issue.

A check in the amount of $870.00 is enclosed with a three-month Request for Extension of Time. This amount is believed to be correct; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

David G. Perryman

David G. Perryman
Registration No. 33,438

NEEDLE & ROSENBERG, P.C.
Suite 1200, The Candler Building
127 Peachtree Street, N.E.
Atlanta, Georgia 30303-1811
(404) 688-0770

Certificate of Mailing

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to:

Commissioner of Patents
and Trademarks
Washington, D.C. 20231

on this 4 day of April, 1995.

David G. Perryman

David G. Perryman

4-4-95

Date

39906_1.WPD

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	)	
	)	
King et al.	)	Art Unit: 1643
	)	
Application No. 07/110,791	)	Examiner: Stephen L. Rawlings
	)	
Filing Date: October 21, 1987	)	Confirmation No. 7373
	)	
For: HUMAN GENE RELATED TO BUT DISTINCT FROM EGF RECEPTOR GENE	)	

AMENDMENT AND RESPONSE

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

BALLARD SPAHR ANDREWS & INGERSOLL, LLP
Customer Number 36339

Sir:

This is responsive to the Office Action dated November 6, 2008.

Amendments to the Specification begin on page 2 of this Amendment.

Amendments to the Claims are reflected in the listing of claims which begins on page 5 of this Amendment.

Remarks begin on page 9 of this Amendment.

Amendments to the Specification

Please amend the specification as follows:

Please replace the paragraph beginning on page 15, line 15 with the following amended paragraph:

COL. 10 LN. 39

DNA fragments containing the AccI-NcoI region (Fig. 1) were digested with either Nco I, Hinf I or Sau 96I (New England Biolabs). These fragments were end-labeled in reactions of 50 µl containing 50 mM Tris-HCl (pH 7.2), 10 mM $MgCl_2$, 0.1 mM dithiothreitol, 50 µg/ml BSA, 10 µCi α^{32}P dxTP (Amersham--where x represents the correct nucleotide for fill-in), 2 units E. coli DNA polymerase large fragment (New England Biolabs). Following labeling, single-stranded material was prepared by electrophoresis. Samples were denatured in 30% dimethyl sulfoxide, 1 mM EDTA and 0.05% bromophenol blue at 90°C for 2 hr. Samples were chilled and electrophoresed in acrylamide gels in a Bethesda Research Labs apparatus. DNA was detected by autoradiography and isolated by elution into 10 mM Tris-HCl (pH 7.0), 1 mM EDTA. Chemical degradation of DNA for sequence analysis was conducted using standard procedures. Cleavage at guanine (G) residues was conducted by reaction with dimethyl sulfonate at 22°C for 10 min. Cleavage at adenine (A) residues was conducted by 12 min reaction at 90°C in 1.5 M NaOH, 1 mM EDTA. Cleavage at cytosine (C) residues was conducted using hydrazine in 2 M NaCl for 13 min at 22°C. Cleavage at thymine (T) residues was conducted using hydrazine with no added NaCl for 10 min at 22°C. Following cleavage, all reactions were twice precipitated using ethanol and thoroughly dried. All samples were reacted with 1 M piperidine at 90°C for 30 min. Piperidine was removed by evaporation in a Savant ~~speed vac~~ SPEEDVAC concentrator. Fragments were separated by electrophoresis in acrylamide gels (BRL HO apparatus) in 8 M urea, 50 mM Tris-borate (pH 8.3), 1 mM EDTA. Detection of degraded ladder was by autoradiography using Kodak XAR5 film at -70°C.

Please replace the paragraph beginning on page 17, line 2 with the following amended paragraph:

High molecular weight DNA (6 µg) from tumor MAC117 (see above) was digested with 12 units restriction enzyme EcoRI (New England Biolabs) in a volume of 100 µl for about one hour at 37°C. DNA was obtained by phenol $CHCl_3$ extraction and ethanol precipitation and resuspended in water at a concentration of 0.1 µg/ml. This DNA (0.2 µg) was ligated to λwes λB

arms (Bethesda Research Labs) (1 μg) using T4 DNA Ligase (New England Biolabs) in a total volume of 20 ml [50 mM Tris-HCl pH 7.4, 10 mM $MgCl_2$ 10 mM dithiothreitol, 0.5 mM spermidine, 1 mM ATP]. This mixture of ligated DNAs was packaged into infectious bacteriophage particles using the ~~Packagene~~ PACKAGENE system (Promega Biotec). These particles were used to infect bacteria BNN45 and about 8 X 10^5 individual phage plaques were obtained.

Please replace the paragraph beginning on page 34, line 20 with the following amended paragraph:

This method involves administering to-the patient one of two types of reagent which preferentially binds cells expressing high levels of the protein product of the erbB-related gene described here. These reagents are either antibodies directed against the protein product or a ligand, which is likely to exist because of the homology of the gene to a growth factor receptor. The ligand is isolated by standard techniques using the intrinsic protein kinase activity of the protein product of the erbB-related gene. Extracts of body fluids and cell culture supernatants are incubated with the protein and γ-^{32}PATP. Thus, provided is a method of detecting amplification or increased expression of a MAC117 gene relative to normal human mammary tissue by reacting a body sample from a patient diagnosed with cancer with antibodies having specific binding affinity for a least a portion of the MAC117 protein product. The presence of ligand is inferred by incorporation of ^{32}P into the protein. The ligand is then purified by standard techniques such as ion exchange chromatography, gel permeation chromatography, isoelectric focusing, gel electrophoresis and the like. The natural ligand or antibody is tagged with one or more agents which will cause injury to cells to which they bind. Such tagging systems include incorporation of radioactive or biological toxins. The present discovery of amplification of the erbB-related gene makes it likely that some tumors carry large amounts of the corresponding protein. Hence, the two type-specific agents will bind in larger amounts to the protein present in the body and thus direct the toxic effects of the reagents to these cells.

Please amend the paragraph at page 21, lines 14-23 as follows:

The availability of cloned probes of the MAC117 gene made it possible to investigate its expression in a variety of cell types. The MAC117 probe detected a single 5-kb transcript in A431 cells (Fig. 4). Under the stringent conditions of hybridization utilized, this probe did not detect any

of the three RNA species recognized by EGF receptor complementary DNA. Provided is a method of detecting amplification of a MAC117 gene, wherein the MAC117 gene contains a nucleotide sequence encoding the amino acids encoded by the 423 nucleotides set forth in Figure 1, in mammary tissue from said patient by hybridizing a nucleic acid derived from breast tissue of said patient with a nucleic acid probe of the MAC117 gene, the amplification of said MAC117 gene relative to normal human breast tissue indicating the presence of human mammary carcinoma in said patient. Thus, MAC117 represents a new functional gene within the tyrosine kinase family, closely related to, but distinct from the gene encoding the EGF receptor.

Col. 12 line 49

With regard to the scope of the Declaration vis-à-vis the scope of the claims, the currently amended claims recite breast cancer, and are not subject to interpretation as disclosing a genus of human cancers. There is evidence in the form of data establishing amplification of MAC117 in breast cancer cells. The Office appears to agree with this where it states the following:

> As apparent from the disclosure of King et al., the cloned gene that was amplified in the nucleic acid of MAC117 cells contains a nucleotide sequence encoding the amino acids encoded by the 423 nucleotides set forth in Figure 1 of this application; see page 975, Figure 2.

Thus, the Declaration establishes that the invention of claims 60 (58), 61 (59), 69 (67) took place prior to the publication of Slamon et al. Overexpression is a typical correlate of amplification, such that the disclosure of amplification is could be reasonably expected to result in increased expression. Thus, the data in the Declaration show that the invention of claims 68-70 was invented prior to the publication date of Slamon et al. Thus, withdrawal of this rejection and allowance of the claims is believed to be merited.

Please charge Deposit Account No. 14-0629 in the amount of $1110.00, representing the fee for a large entity under 37 C.F.R. § 1.17(a)(3), and a Three-Month Extension of Time are enclosed. This amount is believed to be correct; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

BALLARD SPAHR ANDREWS & INGERSOLL, LLP

Gwendolyn D. Spratt
Registration No. 36,016

BALLARD SPAHR ANDREWS & INGERSOLL, LLP
Customer Number 36339
(678) 420-9300 Phone
(678) 420-9301 Fax

CERTIFICATE OF FIRST CLASS MAILING UNDER 37 C.F.R. § 1.8			
I hereby certify that this correspondence, including any items indicated as attached or included, is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date indicated below.			
Name of Person Mailing (Print/Type)	Gwendolyn D. Spratt		
Signature	Gwendolyn D. Spratt	Date	5-6-09